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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,308	02/05/2002	Edgardo Laborde	25352-0027	9701

25213 7590 02/20/2004

HELLER EHRMAN WHITE & MCAULIFFE LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
LIU, HONG	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 02/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,308	LABORDE ET AL.	
	Examiner	Art Unit	
	Hong Liu	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) 1-9 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-9 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 09/03/02.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-9 are pending in this application.

Election/Restrictions

1. Applicant's election without traverse of Group I is acknowledged.

Priority

2. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-9 of this application. There is no disclosure of variable Q nor W being –X-CH2- in the provisional application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following reason(s) apply:

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) the nature

of the invention, 2) the state of the prior art, 3) the predictability of lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein Q can be absent or present. While a number of compounds are disclosed, there is insufficient guidance for preparing additional GlyT2 antagonists which would be effective since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants' claims. Only compounds wherein Q is absent have been made.

Furthermore, no testing data is provided for any of the compounds wherein Q is present in the specification. Examples should be of sufficient scope as to justify the scope of the claim. However, the generic claims are much broader in scope than is represented by the testing. The definitions of the various Q and W variables on the ring system embrace many structurally divergent groups not represented at all in testing, since testing for the instant compounds is not seen in the specification. Markush claims must be provided with support in the disclosure when the "working examples' fail to include written description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See In re Fouch, 169 USPQ 429.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds embraced by the

claims which have not been tested. In cases directed to chemical compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provide by the specification. See In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made that the instant compounds as an entire class have the required activities needed to practice the invention.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability" have been demonstrated to be sufficiently lacking in the instant case for the scope being claimed.

Claims 1-9 are drawn to a method of treating a disease treatable by the inhibition of the glycine transporter 2. The specification reads on any and all disorders such as a nervous disorder, a muscular disorder, psychoses, pain, epilepsy, neurodegenerative diseases, stroke, head trauma, etc. However, in a recent review article on therapeutic glycine transporter inhibitors, Gomeza et al. state that, unlike inhibitors of GlyT-1, the therapeutic potential of GlyT-2 antagonists I is currently being evaluated (see page 680, Current Opinion in Drug Discovery and Development, 2003). The article further states:

> GlyTs have only recently emerged as potential sites of drug action in disorders caused by deficits in inhibitory glycinergic or excitatory NMDA receptor-mediated neurotransmission. In particular , GlyT-1 antagonist appear to have great promise for the treatment of schizophrenia, a widespread psychiatric disease for which no effective medication is currently available. In addition, selective antagonists of GlyT-2 should be useful as novel antispastic and muscle-relaxant, in particular, analgesic compounds that have little effects on higher brain circuits. Efforts to <u>further advance</u> GlyT pharmacology thus appear highly warranted. (p. 680, emphasis added).

The above quote makes it clear that, at least as of 2003, which is a year later than the filing of this application, much more than routine experimentation would be required to find a way to use GlyT2 antagonists to treat pain or spasticity. As of 2002, there was only the "potential", and success would requi future development, i.e. more than routine experimentation.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1). "Optionally substituted" throughout claims 1 and 5 is unclear as to the nature and number of substituent(s) intended.

2). Claim1 is of indeterminate scope for more than one reason. First, no one particular disorder is recited. Second, the claim language may read on diseases not yet fully understood to be affected by glycine transporter antagonists.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(a) as being anticipated by Tobe et al. (WO 01/878855). Tobe teaches the method of using the compound to inhibiting glycine transporter (see Examples in Table 3, page 53).

Claims 1, 2, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Chakravarty et al. (GB 2263635). Chakravarty teaches the method of using the compound to treat CND dysfunctions such as psychoses (see compounds on pages 31-33).

Claims 1, 2, 4, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Gulerman et al. (FARMACO, 1997). Gulerman teaches the method of using the compound to treat CND dysfunctions (see compound 3h on page).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tobe et al. (US 5,506,347). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, page 5 wherein Ring B is substituted aryl, R can be $-[alkyl]_m$-X-Y-R1 wherein X can be S, Y can be a bond, and R1 is aryl, etc. The compounds are taught to be useful as glycine transporter inhibitors. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However,

it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the specie of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. See In re Susi, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in Merck & Co. V. Biocraft Laboratories, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Claims 1, 2, and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chakravarty et al. (GB 2263635). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, page 7 wherein A can be S, R7 is a substituted phenyl, R6 can be aryl or heterocycle, etc. The compounds are taught to be useful in the treatment of certain CND dysfunctions such as psychoses The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the specie of the genus would have similar properties and, thus, the same use as taught for the genus as a whole.

Any inquiry concerning this communication should be directed to Examiner Hong Liu whose telephone number is (571) 272-0669. The examiner can normally be reached on Monday through Friday from 8:30 AM to 6:00 PM.

If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisors, Mukund Shah or James Wilson can be reached at (571) 272-0674 or (571) 272-0661, respectively. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 358-1235.

RICHARD L. RAYMOND
ACTING SPE
ART UNIT 1624

Mukund Shah
Supervisory Patent Examiner
Art Unit 1624

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February 13, 2004